REMARKS

Claim 1 has been amended, new claims 32 and 33 have been added, and claims 13-31 are cancelled in the instant amendment. Claims 8-12 were previously cancelled. Accordingly, claims 1-7, 32, and 33 are pending.

Applicants cancel the claims without prejudice to subsequent revival for prosecution in a divisional or continuation application.

The amendments to the claims add no new matter and are supported throughout the application as filed.

New claim 32 recites a step of selecting a plant that has a selectable marker. Support can be found, *e.g.*, on page 15, lines 9-14.

The rejections will be addressed in the order presented in the Office Action mailed September 10, 2002.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-7 were rejected indefinite. The rejection alleges that claim 1 is unclear as to whether the polypeptide or the polynucleotide is intended to target the gene. Applicants have amended the claim as suggested by the Examiner and therefore respectfully request withdrawal of the rejection.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-7 were rejected as not enabled. The rejection alleges that it would require undue experimentation to develop and evaluate methods of identifying homologous recombination in plants cells with a genetic construct that does not contain a selectable marker gene. Further, the rejection alleges that it would also require undue experimentation to practice the method in a nuclear genome. To the extent that the rejection applies to the amended claims, Applicants respectfully traverse.

The *RBCSB* locus is present on the nuclear genome

First, Applicants note that although the *RBCSB* locus includes three of the four genes encoding the small subunit of RUBISCO, which is involved in photosynthesis, the locus is present in the nuclear genome. The specification indicates that the locus is on Chromosome V (of *Arabidopsis thaliana*) (page 19, line7). Further, the analysis of recombination events was performed using genomic DNA (*see, e.g.,* page 20, lines 3-8). Thus, the examples and guidance provided in the specification are in the context of the nuclear genome.

The claimed methods do not require undue experimentation

Second, the Examiner alleges that it would require undue experimentation to develop and evaluate methods for identifying and obtaining homologous recombination in plant cells transformed with a genetic construct that does not contain a selectable marker gene. In particular the Examiner alleges that the claims are only enabled for a method that comprises a step of growing plants on a selective media prior to the detection of the reporter activity. Applicants disagree.

As the Examiner knows, it is well settled in the biotechnology art that routine screening of even large numbers of samples is not undue experimentation when a probability of success exists. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). As stated in Wands, "enablement is not precluded by the necessity for some experimentation, such as routine screening." *Id.,* 8 USPQ2d at 1404. The claims at issue in *Wands* involved immunoassay methods using high-affinity monoclonal antibodies. An immune response that results in the generation of a particular monoclonal antibody is a complex process. However, the Federal Circuit concluded that it would not require undue experimentation to obtain such antibodies because the methods needed to practice the invention were well known, there was a high level of skill in the art at the time the application was filed, and the Wands disclosure provided considerable direction and guidance on how to practice their invention and presented working examples. *Id.,* 8 USPQ2d at 1406. Thus, even though it might require screening a large number of hybridomas to determine which secretes an antibody with the desired characteristics, the amount of experimentation was not deemed undue by the Court.

The situation here is analogous. Homologous recombination is a complex process. The invention relates to methods of detecting homologous recombination. Applicants have provided examples showing that this screening method works. With respect to the cited art, although both publications discuss the possibility that homologous recombination may be unstable and acknowledges its low frequency, neither publication suggests that homologous recombination simply does not work or cannot be detected.

The specification provides guidance in making and using the fusion polynucleotides used in practicing the invention (*e.g.*, page 13, line 27 through page 14, line 17, which teaches various known reporter sequence that can be used) and working examples. Further, the level of skill in the art is high. Therefore, although it may require screening a large number of samples to identify homologous recombination in view of its low frequency this does not constitute undue experimentation.

The method need not comprise an initial selection step

Applicants note that there are transformation procedures routinely performed in the art that do not require a selectable marker. So-called in planta transformation techniques have been developed that avoid tissue culture and regeneration. Attached as Exhibit 1 is an article (Bent, in *Plant Physiology* 124:1540-1547, 2000) that reviews such techniques, including the vacuum infiltration method of *Arabidopsis* transformation (see, page 1541, 2nd column, 2nd full paragraph) referred to in the "Examples" section of the specification (page 17, lines 11-15). Although such techniques are often performed with a selectable marker, they do not require such a selection step.

In order to expedite prosecution, Applicants also provide a Rule 1.132 Declaration by John G. Jelesko, Ph.D., which provides additional data showing that a step of selecting plants using a selectable marker is not required. Applicants are currently obtaining a signed copy of the Declaration, which will be forwarded to the Examiner as soon as possible.

In the Declaration, Dr. Jelesko describes transformation of *Arabidopsis* to obtain large populations of seedlings containing a synthetic *RBCSB* gene cluster. These plants were

then screened for luciferase activity. Luciferase-positive cells were identified and further characterized for homologous recombination.

Dr. Jelesko indicates that for these experiments, an evaluation of transformation efficiency was also performed based on the kanamycin resistance gene present in the construct. However, he explains that this was conducted using a representative sample of the seed lots and that the seeds that were evaluated for luciferase activity were not subject to such a selection. Thus, although a selectable marker may be present in the construct, it is not required in every instance in order to identify plant cells in which homologous recombination has occurred.

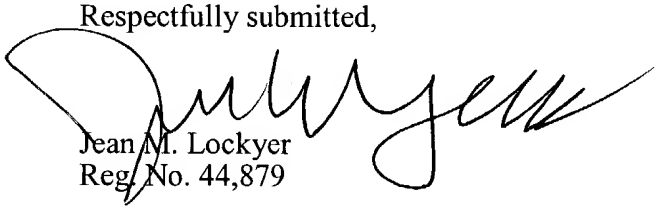
In view of the foregoing, the claims are enabled. Applicants therefore respectfully request withdrawal of the rejection.

CONCLUSION

Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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